# IAP12 Rec'd PCT/PTO 16 MAR 2007

#### IN THE UNITED STATES RECEIVING OFFICE PATENT COOPERATION TREATY

Application No.

: 10/502,470

Confirmation No.

: 4015

Applicant

: Ng et al.

371(c) Date

: July 23, 2004

**Group Art Unit** 

: Not yet assigned

**Examiner:** 

Docket No.

: Not yet assigned

: 007193-5

Customer No.

: 36,234

I hereby certify that, on the date shown below, this correspondence, along with any document stated as being enclosed, is being: deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to Mail Stop PCT, Commissioner for Patents, PO Box 1450, Alexandria VA 22313-1450

Greg McCallum

Mail Stop PCT Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

### TRANSMITTAL OF INFORMATION DISCLOSURE STATEMENT

#### Dear Sir:

The Information Disclosure Statement submitted herewith is being filed within three months of the filing date of the application or date of entry into the national stage of an international application or before the mailing date of a first Office Action on the merits, whichever event occurs last. 37 C.F.R. Section 1.97(b).

Enclosed is Form 1449 and 55 non-patent references. Applicants respectfully request that each of the cited information be expressly considered during the prosecution of this application and that the cited references be made of record therein and appear among the "References Cited" on any patent to issue therefrom. If required, a copy of each reference is attached.

## **FEES**

It is believed no fee is due. If any fee is due, please charge Deposit Account No. 502679.

Reg. No.: 52,492

Tel. No.: 303-828-0655 Fax No.: 303-828-2938 Jennifer M. McCallum, Ph.D., Esq.

Customer No.: 36234

Substitute for form 1449/PTO	Complete if Known	
	Application Number	10/502,470
INFORMATION DISCLOSURE	Filing Date	07/23/2004
STATEMENT BY APPLICANT	First Named Inventor	Aylwin Ng
(llas as many shorts as passagen)	Art Unit	1614
(Use as many sheets as necessary)	Examiner Name	Unknown
Sheet 1 of 7	Attorney Docket Number	007193-05

U.S. Patent Documents					
Examiner Initials*	Cite No. 1	Document Number  Number-Kind Code <sup>2 (f known)</sup>	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

	Foreign Patent Documents				
Examiner Initials*	Cite No. 1	Foreign Patent Document  Number-Kind Code <sup>2 (f known)</sup>	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No. 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s) publisher, city and/or county where published.	T <sup>2</sup>
	1	Ambinder, R. F. et al., "Epstein-Barr virus as a therapeutic target in Hodgkin's	
		disease and nasopharyngeal carcinoma," SEMINARS IN CANCER BIOLOGY,	
		US, Aug 1996, Vol. 7, no. 4, pp. 217-226.	
•	2	Bliek J, Maas Saskia, Ruijter JM, Hennekam RCM, Alders M, Westerveld A and	
		Mannens MAM (2001) Increased tumour risk for BWS patients correlates with	
		aberrant and not methylation: occurance of methylation: occurance of KCNQ10T1	
		hypomethylation in familial cases of BWS. Hum Mol Genet 10: 467-476	
30	3	Brannan CI, et al. (1990) The product of the gene may function as an RNA. Mol &	
0		Cellul Biol 10(1): 28-36	
	4	Brunkow ME and Tilghman SM (1991) Ectopic expression of the gene in mice	
		causes prenatal lethality. Genes Dev 5: 1092-1101	
	5	Busson P, McCoy R, Sadler R, Gilligan K, Tursz T and Raab-Traub N (1992)	
		Consistent transcription of the Epstein-Barr virus LMP2 gene in nasopharyngeal	
		carcinoma. J Virol 66(5): 3257-3262	
	6	Casola S, Pedone, PV, Cavazzana AO, Basso G, Luksch R, d'Amore ES, Carli M,	-
		Bruni CB, Riccio A (1997) Expression and parental imprinting of the gene in	
		human rhabdomyosarcoma. Oncogene 14: 1503-1510	

Examiner	Date	•
Signature	Considered	

Substitute for form 1449/PTO	Complete if Known	
	Application Number	10/502,470
INFORMATION DISCLOSURE	Filing Date	07/23/2004
STATEMENT BY APPLICANT	First Named Inventor	Aylwin Ng
	Art Unit	1614
(Use as many sheets as necessary)	Examiner Name	Unknown
Sheet 2 of 7	Attorney Docket Number	007193-05

Eventions	Cito No. 1	NON PATENT LITERATURE DOCUMENTS  Linguista name of the puther (in CARITAL LETTERS) title of the article (when appropriate) title of the	T <sup>2</sup>
Examiner Initials*	Cite No. 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s) publisher, city and/or county where published.	12
	7	Chen FF, Yan JJ, Lai WW, Jin YT and Su IJ (1998) Epstein- Barr virus-associated	
		nonsmall cell lung carcinoma: as a distinct entity with better prognosis. Cancer	
		82(12): 2334- 2342	
	8	Chien G, Yuen PW, Kwong D and Kwong YL (2001) Comparative genomic	
		hybridization analysis of nasopharygeal carcinoma: consistent patterns of genetic	
:		aberrations and clinicopathological correlations. Cancer Genet. Cytogenet 126: 63-	
		67	
	9	Chow, Lillian S. N. et al., "Effect of p16 <sup>INK4a</sup> on chemosensitivity in	
		nasopharyngeal carcinoma cells," International Journal of Oncology, vol. 17, no.	
		1, July 2000, pp. 135-140.	
	10	Eisen MB, Spellman PT, Brown PO and Botstein D (1998) Cluster analysis and	
		display of genome-wide expression patterns. Proc Natl Acad Sci USA 95: 14863-	!
		14868	
	11	Fang Y, Guan X, Guo Y, Sham J, Deng M, Liang Q, Li H, Zhang H, Zhou H and	
		Trent J (2001) Analysis of genetic alterations in primary nasopharyngeal	
		carcinoma by comparative genomic hybridization. Genes Chromosomes Cancer	
		30: 254-260	
	12	Farrow DC, Vaughan TL, Berwick M, Lynch CF, Swanson GM and Lyon JL	
		(1998) Diet and nasopharyngeal cancer in a low-risk population. Int J Cancer 78:	
		675-679	
	13	Feil R and Khosla S (1999) Genomic imprinting in mammals: an interplay	
		between chromatin and DNA methylation? Trends Genet 15: 431-435	
	14	Feinberg AP (1999) Imprinting of a genomic domain of and loss of imprinting in	
		cancer: an introduction. Cancer Res 59: 1743-1746	
	15	Fioretti F, D, Stoppacciaro A, Ramponi S, Ruco L, Minty A, Sozzani S, Garlanda	
		C, A and Mantovani A (1998) Reduced tumorigenicity and augmented leukocyte	
		infiltration after monocyte chemotactic protein-3 (MCP-3) gene transfer:	

Examiner	Date
Signature	Considered

Substitute for form 1449/PTO	Comp	olete if Known
	Application Number	10/502,470
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	Filing Date	07/23/2004
	First Named Inventor	Aylwin Ng
(II)	Art Unit	1614
(Use as many sheets as necessary)	Examiner Name	Unknown
Sheet 3 of 7	Attorney Docket Number	007193-05

Examiner	Cite No. 1	NON PATENT LITERATURE DOCUMENTS  Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the	T <sup>2</sup>
Initials*	Cite No.	item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s) publisher, city and/or county where published.	-
		perivascular accumulation of dendritic cells in peritumoral tissue and neutrophil	
		recruitment within the tumor. J Immunol 161: 342-346	
	16	Fung, L. F. et al., "Differential gene expression in nasopharyngeal carcinoma	
		cells," LIFE SCIENCES, vol. 67, no. 8, 14 July 2000, pp. 923-936.	
	17	Gray, JW and Collins C (2000) Genome changes and gene expression in human	
		solid tumours. Carcinogenesis 21(3): 443-452	
	18	Hao Y, Crenshaw T, Moulton T, Newcomb E and Tycko B (1993) Tumour-	
		suppressor activity of H19 RNA. Nature 365: 764-767	
	19	Hatada I, Inazawa J, Abe T, Nakayama M, Kaneko Y, Jinno Y, Niikawa N, Ohashi	
		H, Fukushima Y, Iida K, Yutani C, Takahashi S, Chiba Y, Ohishi S and Mukai, T	
		(1996) Genomic imprinting of human p57KIP2 and its reduced expression in	
		Wilms' tumors. Hum Mol. Genet 5(6): 783-788	
	20	Hatada I and Mukai T (1995) Genomic imprinting of p57KIP2, a cyclin-dependent	
		kinase inhibitor, in mouse. Nat Genet 11: 204-206	
	21	Hengstler JG, Pilch H, Schmidt M, Dahlenburg H, Sagemuller J, Schiffer I, Oesch	
		F, Knapstein PG, Kaina B and Tanner B (2001) Metallothionein expression in	
		ovarian cancer in relation to histopathological parameters and molecular markers	
		of prognosis. Int J Cancer 95: 121-127	
	22	Huang DP, Ho JH, Poon YF, Chew EC, Saw D, Lui M, Li CL, Mak LS, Lai SH	
		and Lau (1980) Establishment of a cell line from a differentiated squamous	
		carcinoma of the nasopharynx. Int J Cancer 26: 127-132	
	23	Huang YT, Sheen TS, Chen CL, Lu J, Chang Y, Chen JY and Tsai CH (1999)	
		Profile of cytokine expression in nasopharyngeal carcinomas: a distinct expression	
		of interleukin 1 in tumor and CD4+ T cells. Cancer Res 59: 1599-1605	
	24	Jayasurya A, Bay BH, Yap WM and Tan NG (2000) Correlation of	
		metallothionein expression with apoptosis in nasopharyngeal carcinoma. $Br J$	
		Cancer 82: 1198-1203	

Examiner	Date	
Signature	Considered	

Substitute for form 1449/PTO	Complete if Known	
	Application Number	10/502,470
INFORMATION DISCLOSURE	Filing Date	07/23/2004
STATEMENT BY APPLICANT	First Named Inventor	Aylwin Ng
	Art Unit	1614
(Use as many sheets as necessary)	Examiner Name	Unknown
Sheet 4 of 7	Attorney Docket Number	007193-05

.

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No. 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s) publisher, city and/or county where published.	T <sup>2</sup>
	25	Joyce JA and Schofield PN (1998) Genomic imprinting and cancer. Mol Pathol 51:	
		185-190	
	26	Kim DK, Zhang L, Dzau VJ and Pratt RE (1994) a developmentally regulated	
		gene, is reexpressed in rat vascular smooth muscle cells after injury. J Clin Invest	
		93: 355-360	
	27	Kwong, J. et al., (2002) promoter hypermethylation of multiple genes in	
		nasopharyngeal carcinoma, Clinical Cancer Research 8:131-137.	
	28	Lee AWM, Poon YF, and Foo W (1992) Retrospective analysis of 5037 patients	
		with nasopharyngeal carcinoma treated during 1976-1985. Overall survival and	
		patterns of failure. Int J Radiat Oncol Biol 23(2): 261-270	
	29	Lee J, Gray A, Yuan J, Luoh S-M, Avraham H and Wood WI (1996) Vascular	
		endothelial growth factor-related protein: a ligand and specific activator of the	
		tyrosine kinase receptor Flt4. Proc Natl Acad Sci 93: 1988-1992	
	30	Li E, Beard C and Jaenisch R (1993) Role for DNA methylation in genomic	
		imprinting. Nature 366: 362-365	
	31	Lo, Kwok-Wai et al., "Hypermethylation of the p16 gene in nasopharyngeal	
		carcinoma," Cancer Research, vol. 56, no. 12, 1996, pp. 2721-2725.	
	32	Lo, Kwok-Wai et al, (2001) "High frequency of promoter hypermethylation of	
		RASSF1A in nasopharyngeal carcinoma," Cancer Research, vol. 61 (10): 3877-	
		3881.	
	33	Marks JE, Phillips JL, and Menck HR (1998) The National Cancer Data Base	
		report on the relationship of race and national origin to the histology of	
		nasopharyngeal carcinoma. Cancer 83(3): 582-588.	
	34	Matsuoka S, Edwards MC, Bai C, Parker S, Zhang P, Baldini A, Harper JW and	
		Elledge SJ (1995) p57KIP2, a structurally distinct member of the Cdk inhibitor	
		family, is a candidate tumor suppressor gene. Genes Dev 9: 650-662	

Examiner	Date
Signature	Considered

Substitute for form 1449/PTO	Complete if Known		
	Application Number	10/502,470	
INFORMATION DISCLOSURE	Filing Date	07/23/2004	
STATEMENT BY APPLICANT	First Named Inventor	Aylwin Ng	
(Hanna manual mananan)	Art Unit	1614	
(Use as many sheets as necessary)	Examiner Name	Unknown	
Sheet 5 of 7	Attorney Docket Number	007193-05	

, .

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No. 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s) publisher, city and/or county where published.	T <sup>2</sup>
	35	Moulton T, Crenshaw T, Hao Y, Moosikasuwan J, Lin N, Dembitzer F, Hensle T,	
		Weiss L, McMorrow L, Loew T, et al. (1994) Epigenetic lesions at the locus in	
		Wilms' tumour patients. Nat Genet 7: 440-447	
	36	Mutirangura A, Pornthanakasem W, Theamboonlers A, Sriuranpong V,	
		Lertsanguansinch PVS, Voravud N, Supiyaphun P, and Poorvorawan Y (1998)	
		Epstein-Barr viral DNA in serum of patients with nasopharyngeal carcinoma. Clin	
		Cancer Res 4: 665-669	
	37	Neel HB 3rd (1985) Nasopharyngeal carcinoma. Clinical presentation, diagnosis,	
		treatment, and prognosis. Otolaryngol Clin North Am 18(3): 479-490	
	38	Neel HB (1986) A prospective evaluation of patients with nasopharyngeal	
		carcinoma: an overview. J Otolaryngol 15(3): 137-144	
	39	Pajusola K, Aprelikova Korhonen J, Kaipainen A, Pertovaara L, Alitalo R and	
		Alitalo K (1992) receptor tyrosine kinase contains seven immunoglobulin- like	
		loops and is expressed in multiple human tissues and cell lines. Cancer Res 52:	
		5738-5743	
	40	Paulsen M and Ferguson-Smith AC (2001) DNA methylation in genomic	·
		imprinting, development, and disease. J Pathol 195: 97-110	
	41	Pfeifer K, Philip AL and Tilghman SM (1996) The structural gene is required for	
		transgene imprinting. Proc Natl Acad Sci 93: 13876-13883	
· · · · · · · · · · · · · · · · · · ·	42	Shtivelman E (1997) A link between metastasis and resistance to apoptosis of	
		variant small cell lung carcinoma. Oncogene 14: 2167-2173	
	43	Sigel G, Schillinger M, Henninger K and Bauer G (1994) IgA directed against	
		early antigen of Epstein-Barr virus is no specific marker for the diagnosis of	
		nasopharyngeal carcinoma. J Med Virol 43: 222-227	
	44	Sizhong Z, Xiukung G and Yi Z (1983) Cytogenetic studies on an epithelial cell	
		+line derived from poorly differentiated nasopharyngeal carcinoma. Int J Cancer	
		31: 587-590	
			L

Examiner	Date	
Signature	Considered	

Substitute for form 1449/PTO	Complete if Known	
	Application Number	10/502,470
INFORMATION DISCLOSURE	Filing Date	07/23/2004
STATEMENT BY APPLICANT	First Named Inventor	Aylwin Ng
(1)	Art Unit	1614
(Use as many sheets as necessary)	Examiner Name	Unknown
Sheet 6 of 7	Attorney Docket Number	007193-05

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No.	item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s) publisher, city and/or county where published.	
	45	Sleutels F, Barlow DP and R (2000) The uniqueness of the imprinting mechanism.	
		Curr Opin Genet Dev 10: 229-233	
	46	Taniguchi T, Sullivan ML, Ogawa O and Reeve AE (1995) Epigenetic changes	
		encompassing the 1GF2/H19 locus associated with relaxation of IGF2 imprinting	
		and silencing of H19 in Wilms tumor. Proc Nat1 Acad Sci USA 92: 2159-2163	
	47	Thorvaldsen JL, Duran KL and Bartolomei MS (1998) Deletion of the	
		differentially methylated domain results in loss of imprinted expression of and	
		Igf2. Genes Dev 12: 3693-3702	
	48	Tremblay KD, Duran KL and Bartolomei MS (1997) A kilobase-pair region of the	
		imprinted mouse gene exhibits exclusive paternal methylation throughout	:
		development. Mol Cell Biol 17(18): 4322-4329	
	49	Wang, G. L. et al, "Inhibiting tumorigenic potential by restoration of p16 in	
		nasopharyngeal carcinoma," British Journal of Cancer, Scotland, Dec. 1999, vol.	
		81, no. 7, pp. 1122-1126.	
	50	Wang, Lihong, et al., "Relationship between expression of p16 protein and	
		prognosis in carcinoma of nasopharynx," Journal of West China University of	
		Medical Sciences, vol. 30, no. 4, Dec 1999, pp. 394-396.	
	51	Widschwendter, Martin et al., "The potential prognostic, predictive, and	
		therapeutic values of DNA methylation in cancer," Clinical Cancer Research, Jan	
		2002, vol. 8, no. 1, pp. 17-21.	
<del></del>	52	Williams, HK (2000) Molecular pathogenesis of oral squamous carcinoma. J. Clin	
		Mol Pathol 53: 165-172	
	53	Xiao H, Palhan V, Yang Y and Roeder RG (2000) TIP30 has an intrinsic kinase	
		activity required for up-regulation of a subset of apoptotic genes. EMBO J 19(5):	
		956-963	
			L

Examiner	Date
Signature	Considered

Substitute for form 1449/PTO	Complete if Known		
	Application Number	10/502,470	
INFORMATION DISCLOSURE	Filing Date	07/23/2004	
STATEMENT BY APPLICANT	First Named Inventor	Aylwin Ng	
(1)	Art Unit	1614	
(Use as many sheets as necessary)	Examiner Name	Unknown	
Sheet 7 of 7	Attorney Docket Number	007193-05	

NON PATENT LITERATURE DOCUMENTS				
Examiner Initials*	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s) publisher, city and/or county where published.	T <sup>2</sup>		
	54	Xie, Lu et al., "Identification of differentially expressed genes in nasopharyngeal carcinoma by means of the Atlas human cancer cDNA expression array," <i>Journal of Cancer Research and Clinical Oncology</i> , vol. 126, no.7, July 2000, pp. 400-406.		
	55	Zhan S, Shapiro DN and Helman (1994) Activation of an imprinted allele of the insulin-like growth factor II gene implicated in rhabdomyosarcoma. <i>J Clin Invest</i> 94: 445-448		

Examiner	Date	
Signature	Considered	